AR201-13895B



# The Flavor And Fragrance High Production Volume Consortia

## The Aromatic Consortium

## Robust Summaries for Phenethyl alcohol

**Phenethyl alcohol** **CAS No. 60-12-8**

## FFHPVC Aromatic Consortium Registration Number

**Submitted to the EPA under the HPV Challenge Program by:**

**The Flavor and Fragrance High Production Volume Chemical Consortia**

**1620 I Street, NW, Suite 925**

**Washington, DC 20006**

**Phone: 202-331-2325**

**Fax: 202-463-8998**

# List of Member Companies

**BASF**

**EASTMAN CHEMICAL COMPANY**

**FIRMENICH, INCORPORATED**

**GIVAUDAN CORPORATION**

**HAARMANN & REIMER CORPORATION**

**INTERNATIONAL FLAVOR & FRAGRANCES, INC.**

**KOSA**

**LYONDELL CHEMICAL COMPANY**

**NOVEON, INC.**

**POLAROME INTERNATIONAL**

**PROCTOR & GAMBLE**

**QUEST**

**RHODIA INC.**

**SUMITOMO CHEMICAL COMPANY**

# Table of Contents

# The Flavor and Fragrance High Production Volume Consortia

# Robust Summaries for Phenethyl alcohol

The evaluation of the quality of the following data uses a systematic approach described by Klimisch [Klimisch *et al*., 1996]. Based on criteria relating to international testing standards for categorizing data reliability, four reliability categories have been established. The following categories are:

- Reliability code 1. Reliable without restrictions
- Reliability code 2. Reliable with restrictions
- Reliability code 3. Not reliable
- Reliability code 4. Not assignable

# 1 CHEMICAL AND PHYSICAL PROPERTIES

## 1.1 Melting Point

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Colorless liquid |
| **Method/guideline** | Measured |
| **GLP** | Ambiguous |
| **Melting Point** | -27 °C |
| **Decomposition** | No |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Basic data given: comparable to guidelines/standards. |
| **References** | CRC Handbook of Chemistry and Physics (1986) 67th edition, Robert C. Weast, editor, The Chemical Rubber Co Press, Inc. Boca Raton, FL. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Measured |
| **Melting Point** | -27 °C |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Basic data given: comparable to guidelines/standards. |
| **References** | Merck Index (1996) 12th edition, Susan Budavari, editor, Merck & Co. Inc. Whitehouse Station, NJ. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Calculated/adapted Joback method |
| **Melting Point** | -6 °C |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Calculated. |
| **References** | MPBPVP EPI Suite (2000a) US Environmental Protection Agency. |

## 1.2 Boiling Point

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Measured |
| **GLP** | Ambiguous |
| **Boiling Point** | 218.2 °C |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Basic data given: comparable to guidelines/standards. |
| **References** | CRC Handbook of Chemistry and Physics (1986) 67th edition, Robert C. Weast, editor, The Chemical Rubber Co Press, Inc. Boca Raton, FL. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Measured |
| **Boiling Point** | 219 - 221 °C |
| **Pressure** | 750 mm Hg |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Basic data given: comparable to guidelines/standards. |
| **References** | Merck Index (1996) 12th edition, Susan Budavari, editor, Merck & Co. Inc. Whitehouse Station, NJ. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Calculated/adapted Stein and Brown method |
| **Boiling Point** | 224.8 °C |
| **Pressure** | 750 mm Hg |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Calculated. |
| **References** | MPBPVP EPI Suite (2000a) US Environmental Protection Agency. |

## 1.3 Vapor Pressure

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Measured |
| **GLP** | Ambiguous |
| **Year** | 1995 |
| **Remarks for Test Conditions** | Study was conducted at 30 °C, skin temperature |
| **Vapor Pressure** | 0.0707 mm Hg |
| **Temperature** | 30 °C |
| **Data Qualities Reliabilities** | Reliability code 1. Reliable without restriction. |

| | |
|---|---|
| **Remarks for Data Reliability** | Code 1. Comparable to guideline study. |
| **References** | Vuilleumier C., Flament I., and Sauvegrain P. (1995) Headspace analysis study of evaporation rate of perfume ingredients applied to skin. Inter. J. of Cos. Sci., 17, 61-76. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Measured |
| **Vapor Pressure** | 0.0868 mm Hg |
| **Temperature** | 25 °C |
| **Data Qualities Reliabilities** | Reliability code 1. Reliable without restriction. |
| **Remarks for Data Reliability** | Code 1. Comparable to guideline study. |
| **References** | MPBPVP EPI Suite (2000b) US Environmental Protection Agency (Daubert T.E. and Danner, R.P., 1989). |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Calculated/modified Grain method |
| **Vapor Pressure** | 0.0222 mm Hg |
| **Temperature** | 25 °C |
| **Remarks for Test Conditions** | Based on input parameters: boiling point - 218.2 °C. |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Calculated. |
| **References** | MPBPVP EPI Suite (2000a) US Environmental Protection Agency. |

## 1.4 n-Octanol/Water Partition Coefficients

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Experimental |
| **GLP** | Not applicable |

| | |
|---|---|
| **Log Pow** | 1.36 |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Basic data given: comparable to guidelines/standards. |
| **References** | Sangster J. (1989) Octanol-water partition coefficients of simple organic compounds. J Phys. Chem. Ref. Data, 18(3), 1111-1229. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Measured |
| **Log Pow** | 1.36 |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Basic data given: comparable to guidelines/standards. |
| **References** | KOWWIN EPI Suite (2000b) US Environmental Protection Agency (Hansch C. *et al*., 1995). |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Calculated/KOWWIN |
| **Log Pow** | 1.57 |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable |
| **Remarks for Data Reliability** | Code 4. Calculated. |
| **References** | KOWWIN EPI Suite (2000a) US Environmental Protection Agency. |

## 1.5 Water Solubility

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/Guideline** | Measured |
| **Value (mg/L) at Temperature** | 22,200 mg/L at 25 °C |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |

| | |
|---|---|
| **Remarks for Data Reliability** | Code 2. Basic data given: comparable to guidelines/standards. |
| **References** | WSKOWIN EPI Suite (2000b) US Environmental Protection Agency (Vivandi S.C. *et al*., 1981) |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/Guideline** | Measured |
| **Value (mg/L) at Temperature** | 20,340 mg/L |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Basic data given: comparable to guidelines/standards. |
| **References** | Merck Index (1996) 12th edition, Susan Budavari, editor, Merck & Co. Inc. Whitehouse Station, NJ. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/Guideline** | Calculated |
| **Value (mg/L) at Temperature** | 3272 mg/L at 25 °C |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Calculated. |
| **References** | WSKOWIN EPI Suite (2000a) US Environmental Protection Agency). |

# 2 ENVIRONMENTAL FATE AND PATHWAYS

## 2.1 Photodegradation

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Calculated |
| **Test Type** | AOPWIN |
| **Halflife t1/2** | 12.6 hours |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Calculated. |
| **References** | AOPWIN EPI Suite (2000) U S Environmental Protection Agency. |

## 2.2 Biodegradation

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | 99.0% pure |
| **Method** | OECD Guideline 301B |
| **Test Type** | Sealed vessel carbon dioxide production test |
| **GLP** | Yes |
| **Year** | 1994 |
| **Contact Time** | 28 days |
| **Innoculum** | Secondary effluent from an unacclimatized activated sludge plant at URL north. |
| **Remarks for Test Conditions** | Test material was directly added to the incubation mixture. The incubation was 28 days. The nominal concentration was 10 mg/l organic carbon. The test temperature range was 17-22 °C. |
| **Degradation % After Time** | 106.3% after 28 days |
| **Remarks Results** | Biodegradation was 106.3% (103.3%-109.2%). |

| | |
|---|---|
| **Time required for 10% degradation** | 1 day |
| **10 day window criteria** | Yes |
| **Total degradation** | Yes |
| **Classification** | Readily and ultimately biodegradable |
| **Conclusion Remarks** | Phenethyl alcohol was shown to be readily and ultimately biodegradable. |
| **Data Qualities Reliabilities** | Reliability code 1. Reliable without restriction. |
| **Remarks for Data Reliability** | Code 1. Guideline study. |
| **Reference** | Quest International Ltd. (1994) The ultimate biodegradability of phenylethyl alcohol in the sealed vessel test. Unpublished report. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Calculated |
| **Test Type** | BIOWIN |
| **Results** | Probability of Rapid Biodegradation 1.03 (Linear Model) - 0.99 (Non-Linear). MITI Model 0.54 (Linear Model) - 0.71 (Non-Linear) |
| **Conclusion Remarks** | Expert Survey Biodegradation Results: Ultimate Survey Model: 3.0 (weeks) - Primary Survey 3.7 (days to weeks) |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Calculated. |
| **Reference** | BIOWIN EPI Suite (2000) US Environmental Protection Agency. |

## 2.3 Fugacity

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Model Conditions** | 1000 kg/hr emissions |
| **Test Type** | Environmental Equilibrium Partitioning Model |
| **Method** | Mackay |
| **Model Used** | Level III |

| | |
|---|---|
| **Input Parameters** | MW, VP, log Kow, MP, water solubility, Henry's LC |
| **Media** | Air |
| **Model Data and Results** | Half-life = 25.3 hours |
| **Estimated Distribution and Media Concentration** | 2.3% |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Calculated. The data are obtained by a recognized fugacity calculation method. |
| **References** | Mackay D., A. DiGuardo, S. Paterson, G. Kicsi and C.E. Cowan (1996a) Assessing the fate of new and existing chemicals: a five stage process. Environmental Toxicology and Chemistry, 15(9), 1618-1626.<br><br>Mackay D., A. DiGuardo, S. Paterson and C.E. Cowan (1996b) Evaluating the fate of a variety of types of chemicals using the EQC model. Environmental Toxicology and Chemistry, 15(9), 1627-1637. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Model Conditions** | 1000 kg/hr emissions |
| **Test Type** | Environmental Equilibrium Partitioning Model |
| **Method** | Mackay |
| **Model Used** | Level III |
| **Input Parameters** | MW, VP, log Kow, MP, water solubility, Henry's LC |
| **Media** | Water |
| **Model Data and Results** | Half-life = 360 hours |
| **Estimated Distribution and Media Concentration** | 46% |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Calculated. The data are obtained by a recognized fugacity calculation method. |
| **References** | Mackay D., A. DiGuardo, S. Paterson, G. Kicsi and C.E. Cowan (1996a) Assessing the fate of new and existing chemicals: a five stage process. Environmental Toxicology and Chemistry, 15(9), 1618-1626.<br><br>Mackay D., A. DiGuardo, S. Paterson and C.E. Cowan (1996b) Evaluating the fate of a variety of types of chemicals using the EQC model. Environmental Toxicology and Chemistry, 15(9), |

1627-1637.

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Model Conditions** | 1000 kg/hr emissions |
| **Test Type** | Environmental Equilibrium Partitioning Model |
| **Method** | Mackay |
| **Model Used** | Level III |
| **Input Parameters** | MW, VP, log Kow, MP, water solubility, Henry's LC |
| **Media** | Soil |
| **Model Data and Results** | Half-life = 360 hours |
| **Estimated Distribution and Media Concentration** | 51.6% |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Calculated. The data are obtained by a recognized fugacity calculation method. |
| **References** | Mackay D., A. DiGuardo, S. Paterson, G. Kicsi and C.E. Cowan (1996a) Assessing the fate of new and existing chemicals: a five stage process. Environmental Toxicology and Chemistry, 15(9), 1618-1626.<br>Mackay D., A. DiGuardo, S. Paterson and C.E. Cowan (1996b) Evaluating the fate of a variety of types of chemicals using the EQC model. Environmental Toxicology and Chemistry, 15(9), 1627-1637. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Model Conditions** | 1000 kg/hr emissions |
| **Test Type** | Environmental Equilibrium Partitioning Model |
| **Method** | Mackay |
| **Model Used** | Level III |
| **Input Parameters** | MW, VP, log Kow, MP, water solubility, Henry's LC |
| **Media** | Sediment |
| **Model Data and Results** | Half-life = 1440 hours |

| | |
|---|---|
| **Estimated Distribution and Media Concentration** | 0.09% |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Calculated. The data are obtained by a recognized fugacity calculation method. |
| **References** | Mackay D., A. DiGuardo, S. Paterson, G. Kicsi and C.E. Cowan (1996a) Assessing the fate of new and existing chemicals: a five stage process. Environmental Toxicology and Chemistry, 15(9), 1618-1626.<br><br>Mackay D., A. DiGuardo, S. Paterson and C.E. Cowan (1996b) Evaluating the fate of a variety of types of chemicals using the EQC model. Environmental Toxicology and Chemistry, 15(9), 1627-1637. |

# 3 ECOTOXICITY

## 3.1 Acute Toxicity to Fish

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Purity greater than 99.5% |
| **Method/guideline** | DIN 38 412 96 hour static toxicity |
| **Test Type** | Experimental |
| **GLP** | No |
| **Year** | 1988 |
| **Species/Strain/Supplier** | Golden Orfe (*Leuciscus idus*) |
| **Exposure Period** | 96 hours |
| **Analytical monitoring** | None |
| **Remarks for Test Conditions** | Reconstituted fresh water according to guideline, 10 L at 21 °C. 10 fish/concentration. Appropriate statistical analyses were performed. |
| **Reference substances** | Chloroacetamide |
| **Observations of Precipitation** | No evidence of precipitation. |
| **Endpoint value** | LC50 = 220-460 mg/L |
| **Nominal concentrations as mg/L** | 100, 215, 464, 1000 mg/L |
| **Remarks fields for results** | 100% mortality at high dose after 1 hour and at 464 mg/L after 24 hour. No mortality at 2 lower concentrations. |
| **Unit** | mg/L |
| **Conclusion Remarks** | LC50 = 220-460 mg/L |
| **Data Qualities Reliabilities** | Reliability code 1. Reliable without restriction. |
| **Remarks for Data Reliability** | Code 1. Guideline study. |
| **Reference** | BASF AG (1988c) Abteilung Toxikologie unpublished data. (87/410). |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |

| | |
|---|---|
| **CAS No.** | 60-12-8 |
| **Method/guideline** | ECOSAR |
| **Test Type** | Calculated |
| **GLP** | Not Applicable |
| **Species/Strain/Supplier** | Fish |
| **Exposure Period** | 96 hour |
| **Remarks for Test Conditions** | Based on: melting point = -27 C; water solubility = 22,200 mg/L; KOW = 1.57. |
| **Endpoint value** | LC50 = 230 mg/L |
| **Conclusion Remarks** | LC50 = 230 mg/L |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Calculated. |
| **Reference** | ECOSAR EPI Suite (2000) US Environmental Protection Agency, OPPT Risk Assessment Division (G. Cash & V. Nabholz, April 2001). |

## 3.2 Acute Toxicity to Aquatic Invertebrates

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Purity greater than 99% |
| **Method/guideline** | EPA EG1, 1982 |
| **Test Type** | Experimental |
| **GLP** | No |
| **Year** | 1988 |
| **Species/Strain/Supplier** | *Daphnia magna Straus* |
| **Analytical procedures** | None |
| **Test Details** | 48 hours |
| **Nominal concentrations as mg/L** | 31.25, 62.5, 125,250, 500 |
| **EC50, EL50, LC0, at 24,48 hours** | 24 hour EC50 330 mg/L; 48 hour EC50 287 mg/L |
| **Conclusion remarks** | 48 hour EC0 125 mg/L; EC100 500 mg/L |

| | |
|---|---|
| **Biological observations** | Inability to swim |
| **Appropriate statistical evaluations?** | Yes |
| **Data Qualities Reliabilities** | Code 1. Guideline study. |
| **Data Reliability Remarks** | Reliability code 1. Reliable without restriction. |
| **Reference** | BASF AG (1988a) Labor Oekologie. Unpublished report (0107/88). |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | ECOSAR |
| **Test Type** | Calculated |
| **Species/Strain/Supplier** | *Daphnia magna* |
| **Test Details** | 48 hours |
| **Remarks for Test Conditions** | Based on: melting point = -27 C; water solubility = 22,200 mg/L; KOW = 1.57. |
| **EC50, EL50, LC0, at 24,48 hours** | LC50 = 239 mg/L |
| **Conclusion remarks** | LC50 = 239 mg/L |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Data Reliability Remarks** | Code 4. Calculated. |
| **Reference** | ECOSAR EPI Suite (2000) US Environmental Protection Agency, OPPT Risk Assessment Division (G. Cash & V. Nabholz, April 2001). |

## 3.3 Acute Toxicity to Aquatic Plants

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Experimental |
| **Test Type** | 72 hour growth inhibition test |
| **GLP** | No |
| **Year** | 1988 |
| **Species/Strain/Supplier** | *Scenedesmus subspicatus subspicatus* |

| | |
|---|---|
| **Exposure Period** | 72 hour |
| **Nominal concentrations as mg/L** | 200, 280, 400, 560, 800, 1600 |
| **NOEC, LOEC or NOEL, LOEL** | NOEC 280 |
| **Biological observations** | Biomass |
| **Conclusion Remarks** | EC10 - 300; EC50 - 490; EC90 - 790 |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Acceptable, well-documented publication/study report that meets basic scientific principles. |
| **Reference** | BASF AG (1988b) Labor Oekologie, Unpublished data (1010/88). |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Calculated |
| **Test Type** | ECOSAR |
| **GLP** | Not Applicable |
| **Species/Strain/Supplier** | Green algae |
| **Exposure Period** | 96 hour |
| **Remarks for Test Conditions** | Based on: melting point = -27 C; water solubility = 22,200 mg/L; KOW = 1.57. |
| **Endpoint value** | EC50 = 146 mg/L |
| **Conclusion Remarks** | EC50 = 146 mg/L |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Calculated. |
| **Reference** | ECOSAR EPI Suite (2000) US Environmental Protection Agency, OPPT Risk Assessment Division (G. Cash & V. Nabholz, April 2001). |

# 4 HUMAN HEALTH TOXICITY

## 4.1 Acute Toxicity

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute oral LD50 study |
| **GLP** | Ambiguous |
| **Year** | 1982 |
| **Species/strain** | Rat/Sprague-Dawley |
| **Sex** | Male and Female |
| **# of animals per sex per dose** | 5 |
| **Vehicle** | 0.25% methylcellulose |
| **Route of Administration** | Oral-Gavage |
| **Remarks for Test Conditions** | Test material in 0.25% methylcellulose was given to groups of 10 (5/sex) Sprague-Dawley rats at 1000, 1600, 2000, 2500 & 3200 mg/kg following an 18 hour fast. Animals were observed immediately and at 1, 4 & 24 hours after dose & 2times/day for 14 days. LD50 with 95% confidence limits was determined by method of Litchfield and Wilcoxon (1949). Could not calculate the LD50 for females according to this method. |
| **Value LD50 or LC50 with confidence limits** | Male rat LD50 = 1692.9 mg/kg with 95% C.I. 1433.3-1998.9 mg/kg. Calculated LD50 for male and female rats = 1609 mg/kg 95% C.I. Of 1399.6-1850.4 mg/kg. |
| **Number of deaths at each dose level** | 1000 mg/kg: No deaths; 1600mg/kg: 5/10 dead; 2000 mg/kg: 9/10 dead; 2500 mg/kg: 10/10 dead. |
| **Conclusion Remarks** | The oral LD50 in male and female rats was reported to be 1609 mg/kg 95% C.I. of 1399.6-1850.4 mg/kg. |
| **Data Qualities Reliabilities** | Reliability code 1. Reliable without restriction. |
| **Remarks for Data Reliability** | Code 1. Comparable to guideline study. |
| **References** | International Flavors & Fragrances, Inc. (1982) Acute oral toxicity study of phenethyl alcohol in rats. Unpublished report. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |

| | |
|---|---|
| **Test Type** | Acute oral LD50 study |
| **GLP** | No |
| **Year** | 1974 |
| **Species/strain** | Rat |
| **Sex** | Not reported |
| **Route of Administration** | Oral |
| **Value LD50 or LC50 with confidence limits** | Reported LD50 = 2.46 ml/kg or 2509 mg/kg |
| **Conclusion Remarks** | The oral LD50 for phenethyl alcohol in rats was reported to be 2.46 (1.79-3.39) ml/kg. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles. Published in a peer-reviewed journal. |
| **References** | Carpenter C.P., Weil, C.S., and Smyth, H.F. (1974) Range-finding toxicity data: List VIII. Toxicology and Applied Pharmacology, 28, 313-319. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute oral LD50 study |
| **GLP** | No |
| **Year** | 1963 |
| **Species/strain** | Rats/Osborne-Mendel |
| **Sex** | Male and Female |
| **Route of Administration** | Oral-Gavage |
| **Value LD50 or LC50 with confidence limits** | LD50 = 1790 mg/kg. 95% C.I. 1580-2020 mg/kg; Slope = 1.2 (1.1-1.3). |
| **Number of deaths at each dose level** | Death from 4 to 18 hours. |
| **Remarks for Test Conditions** | Animals were subjected to an 18-hour predose fast. All doses were given by intubation. The animals were observed over a 2-week period for mortality and/or systemic effects. LD50 results were calculated per Litchfield-Wilcoxon (1949). No necropsy mentioned |
| **Remarks for Results** | Toxic signs were coma within 15 minutes. Gross pathology showed irritation of the lower half of the stomach on the higher doses. |

| | |
|---|---|
| **Conclusion Remarks** | The oral LD50 in rats was calculated to be 1790 mg/kg. 95% C.I. 1580-2020 mg/kg; Slope = 1.2 (1.1-1.3).<br>Study was conducted prior to GLP or OECD guidelines but was reported by respected researchers at the FDA and published in a peer-reviewed journal. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles. Published in a peer-reviewed journal. |
| **References** | Jenner P.M., Hagan, E.C., Taylor, J.M., Cook, E.L. and Fitzhugh, O.G. (1964) Food flavorings and compounds of related structure I. Acute oral toxicity. Food and Cosmetics Toxicology, 2(3), 327-343. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute oral LD50 study |
| **GLP** | Ambiguous |
| **Year** | 1982 |
| **Species/strain** | Rat/Wistar |
| **Sex** | Male |
| **# of animals per sex per dose** | 10 |
| **Vehicle** | None |
| **Route of Administration** | Oral |
| **Remarks for Test Conditions** | Animals were observed for 14 days. |
| **Value LD50 or LC50 with confidence limits** | Reported LD50 = 1500 mg/kg (C.I. 1200-2000 mg/kg) |
| **Number of deaths at each dose level** | Dose 760 mg/kg: 1/10 dead; 1200 mg/kg: 1/10 dead; 1900 mg/kg: 9/10 1.9 dead; 5000 mg/kg: 10/10 dead. |
| **Conclusion remarks** | The oral LD50 for phenethyl alcohol was calculated to be 1500 mg/kg (C.I. 1200 - 2000 mg/kg) in rats. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Comparable to guideline study with acceptable restrictions. |
| **References** | Moreno O. M. (1982a) Acute toxicity studies. Unpublished report to RIFM. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute oral LD50 study |
| **GLP** | No |
| **Year** | 1974 |
| **Species/strain** | Rat |
| **Sex** | Male and Female |
| **# of Animals per Sex per Dose** | 6 males and 5 females |
| **Vehicle** | Sunflower oil |
| **Route of Administration** | Oral-Gavage |
| **Remarks for Test Conditions** | 15-day observation period. Vehicle was sunflower oil. |
| **Value LD50 or LC50 with confidence limits** | Reported LD50 = 2540 mg/kg |
| **Conclusion Remarks** | The acute oral LD50 in rats was reported to be 2540 mg/kg. |
| **Data Qualities Reliabilities** | Reliability code 3. Not reliable. |
| **Remarks for Data Reliability** | Code 3. Documentation insufficient for assessment. |
| **References** | Zaitsev A.N. and Rakhmanina, N.L. (1974) Some data on the toxic properties of phenylethanol and cinnamic alcohols. Vop. Pitan, 6, 48-53. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute oral LD50 study |
| **GLP** | No |
| **Year** | 1974 |
| **Species/strain** | Mice |
| **Sex** | Male and Female |
| **# of animals per sex per dose** | 6 males and 5 females |
| **Vehicle** | Sunflower oil |
| **Route of Administration** | Oral-Gavage |
| **Remarks for Test Conditions** | 15-day observation period. Vehicle was sunflower oil. |

| | |
|---|---|
| **Value LD50 or LC50 with confidence limits** | Reported LD50 = 2540 mg/kg. |
| **Conclusion Remarks** | The acute oral LD50 in mice was reported to be 2540 mg/kg. |
| **Data Qualities Reliabilities** | Reliability code 3. Not reliable. |
| **Data Reliabilities Remarks** | Code 3. Documentation insufficient for assessment. |
| **References** | Zaitsev A.N. and Rakhmanina, N.L. (1974) Some data on the toxic properties of phenylethanol and cinnamic alcohols. Vop. Pitan, 6, 48-53. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute oral LD50 study |
| **GLP** | No |
| **Year** | 1963 |
| **Species/strain** | Mice |
| **Sex** | Not reported |
| **Route of Administration** | Oral |
| **Remarks for Test Conditions** | Not reported |
| **Value LD50 or LC50 with confidence limits** | Reported LD50 = 800 -1500 mg/kg |
| **Number of deaths at each dose level** | Not reported |
| **Conclusion Remarks** | The acute oral LD50 in mice was reported to be 800 -1500 mg/kg. |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4. Only secondary literature (review, tables, books, etc.). |
| **References** | Fassett D.W. (1963) Personal communication. In Industrial Hygiene and Toxicology, 1476-1477. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute oral LD50 study |
| **GLP** | No |
| **Year** | 1974 |

| | |
|---|---|
| **Species/strain** | Guinea pig |
| **Sex** | Male and Female |
| **# of animals per sex per dose** | 6 males and 5 females |
| **Route of Administration** | Oral-Gavage |
| **Vehicle** | Sunflower oil |
| **Value LD50 or LC50 with confidence limits** | Reported LD50 = 2540 mg/kg |
| **Remarks for test conditions** | 15-day observation period. Vehicle was sunflower oil. |
| **Conclusion Remarks** | The acute oral LD50 in guinea pig was reported to be 2540 mg/kg. |
| **Data Qualities Reliabilities** | Reliability code 3. Not reliable. |
| **Remarks for Data Reliability** | Code 3. Documentation insufficient for assessment. |
| **References** | Zaitsev A.N. and Rakhmanina, N.L. (1974) Some data on the toxic properties of phenylethanol and cinnamic alcohols. Vop. Pitan, 6, 48-53. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute oral LD50 study |
| **GLP** | No |
| **Year** | 1963 |
| **Species/strain** | Guinea pig |
| **Sex** | Not reported |
| **# of animals per sex per dose** | Not reported |
| **Route of Administration** | Oral |
| **Vehicle** | Not reported |
| **Value LD50 or LC50 with confidence limits** | Calculated LD50 = 400 - 800 mg/kg |
| **Conclusion Remarks** | The acute oral LD50 value in guinea pig was calculated to be 400 - 800 mg/kg. |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4.Only secondary literature (review, tables, books, etc.). |
| **References** | Fassett D.W. (1963) Personal communication. In Industrial Hygiene and Toxicology, 1476-1477. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute dermal LD50 study |
| **GLP** | No |
| **Year** | 1974 |
| **Species/strain** | Rabbit |
| **Sex** | Not reported |
| **Route of Administration** | Dermal |
| **Value LD50 or LC50 with confidence limits** | Reported LD50 = 0.79 ml/kg or 805 mg/kg |
| **Conclusion Remarks** | The dermal LD50 for phenethyl alcohol in rabbits was reported to be 0.79 ml/kg (0.49-1.30) ml/kg. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Data Reliabilities Remarks** | Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles. Published in a peer-reviewed journal. |
| **References** | Carpenter C.P., Weil, C.S., and Smyth, H.F. (1974) Range-finding toxicity data: List VIII. Toxicology and Applied Pharmacology, 28, 313-319. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute dermal LD50 study |
| **GLP** | Yes |
| **Year** | 1982 |
| **Species/strain** | Rat |
| **Sex** | Not reported |
| **# of animals per sex per dose** | 10 |
| **Route of Administration** | Dermal |
| **Remarks for Test Conditions** | 5000 mg/kg was applied to the rat skin |
| **Value LD50 or LC50 with confidence limits** | LD50 greater than 5000 mg/kg |
| **Number of deaths at each dose level** | None |

| | |
|---|---|
| **Conclusion Remarks** | The dermal LD50 in rat was reported to be greater than 5000 mg/kg. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Comparable to guideline study with acceptable restrictions. |
| **References** | Moreno O. M. (1982b) Acute toxicity studied. Unpublished report to RIFM. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute dermal LD50 study |
| **GLP** | Ambiguous |
| **Year** | 1983 |
| **Species/strain** | Rabbits/New Zealand white |
| **Sex** | Male and Female |
| **# of animals per sex per dose** | 4 |
| **Route of Administration** | Dermal |
| **Value LD50 or LC50 with confidence limits** | LD50 = 2535 mg/kg (C.I. 1769-3634 mg/kg). |
| **Remarks for Test Conditions** | Test material at 1600, 2500 and 4000 mg/kg was applied to abraded and intact skin of groups of 8 (4/sex) New Zealand white rabbits. Test sites were washed after 24 hours. Observations recorded 2 & 4 hour later & twice daily thereafter for 14 days. |
| **Number of deaths at each dose level** | 1600 mg/kg: 1/8 died; 2500 mg/kg: 5/8 died; 4000 mg/kg: 6/8 died. |
| **Conclusion Remarks** | The acute dermal LD50 value in rabbits was calculated to be 2535 mg/kg. |
| **Data Qualities Reliabilities** | Reliability code 1. Reliable without restriction. |
| **Remarks for Data Reliability** | Code 1. Comparable to guideline study. |
| **References** | International Flavors & Fragrances, Inc. (1983) Acute dermal toxicity test of phenethyl alcohol in rabbits. Unpublished report. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute intraperitoneal LD50 study |

| | |
|---|---|
| **GLP** | No |
| **Year** | 1963 |
| **Species/strain** | Mice |
| **Sex** | Not reported |
| **# of animals per sex per dose** | Not reported |
| **Route of Administration** | Intraperitoneal |
| **Value LD50 or LC50 with confidence limits** | Reported LD50 = 200 - 400 mg/kg |
| **Conclusion Remarks** | The intraperitoneal LD50 value in mice was reported to be 200 - 400 mg/kg. |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4.Only secondary literature (review, tables, books, etc.). |
| **References** | Fassett D.W. (1963) Personal communication. In Industrial Hygiene and Toxicology, 1476-1477. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute intraperitoneal LD50 study |
| **GLP** | No |
| **Year** | 1963 |
| **Species/strain** | Guinea pig |
| **Sex** | Not reported |
| **# of animals per sex per dose** | Not reported |
| **Route of Administration** | Intraperitoneal |
| **Value LD50 or LC50 with confidence limits** | Calculated LD50 = 400 - 800 mg/kg |
| **Conclusion Remarks** | The intraperitoneal LD50 in guinea pig was calculated to be 400 - 800 mg/kg. |
| **Data Qualities Reliabilities** | Reliability code 4. Not assignable. |
| **Remarks for Data Reliability** | Code 4.Only secondary literature (review, tables, books, etc.). |
| **References** | Fassett D.W. (1963) Personal communication. In Industrial Hygiene and Toxicology, 1476-1477. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Acute inhalation LC50 study. |
| **GLP** | Ambiguous |
| **Year** | 1980 |
| **Species/strain** | Rat/Sprague-Dawley |
| **Sex** | Male and Female |
| **# of animals per sex per dose** | 5 |
| **Vehicle** | Aerosol |
| **Route of Administration** | Inhalation |
| **Remarks for Test Conditions** | After a 4-hour exposure the following observations were made over a 14-day period: mortality, clinical signs, body weight, gross and histopathology. |
| **Value LD50 or LC50 with confidence limits** | Acute inhalation LC50 was reported to be greater than 4.63 mg/L. |
| **Number of deaths at each dose level** | 0/10 at 4.63 mg/L |
| **Remarks for Results** | The animals exhibited no clinical signs during or up to 14 days after exposure at 4.63 mg/L. |
| **Conclusion Remarks** | Acute inhalation LC50 for phenethyl alcohol in rats was reported to be greater than 4.63 mg/L. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Comparable to guideline study with acceptable restrictions. |
| **References** | Breckenridge C., C.J.Collins, S.Qureshi and B.G.Procter (1980) The acute toxicity of inhaled phenyl ethyl alcohol in the albino rat. Unpublished report to RIFM. |

## 4.2 Genetic Toxicity

### 4.2.1 *In vitro* genotoxicity

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Purity greater than 97% |

| | |
|---|---|
| **Method/guideline** | Ames test |
| **Test Type** | Reverse mutation |
| **System of Testing** | Bacterial |
| **GLP** | No |
| **Year** | 1980 |
| **Species/Strain** | *Salmonella typhimurium* strains TA98, TA100, TA1535 & TA1537 |
| **Metabolic Activation** | With and without S9 fraction rat liver treated with Aroclor 1254 |
| **Doses/Concentration** | 3 micromol/plate |
| **Statistical Methods** | Not given |
| **Remarks for Test Conditions** | The solvent used was ethanol. Only one replicate was performed for the substances, which tested negative. Similar to OECD 471. No *E. coli* strain was included. |
| **Results** | No effects |
| **Cytotoxic concentration** | Not given |
| **Genotoxic Effects** | None |
| **Appropriate Statistical Evaluations** | None given |
| **Conclusion Remarks** | No mutagenic activity of phenethyl alcohol was observed using *Salmonella typhimurium* strains TA98, TA100, TA1535 & TA153 in the presence or absence of S9 fraction. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Comparable to guideline study with acceptable restrictions. Published in a peer-reviewed journal. |
| **References** | Florin I., Rutberg, L., Curvall, M. and Enzell, C. R. (1980) Screening of tobacco smoke constituents for mutagenicity using the Ames' test. Toxicology, 18, 219-232. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Purity greater than 98% |
| **Method/guideline** | *In Vitro* Chromosome Aberration Test with Human Lymphocytes |
| **Test Type** | Sister Chromatid Exchange |
| **System of Testing** | Human lymphocytes |
| **GLP** | No |

| | |
|---|---|
| **Year** | 1983 |
| **Species/Strain** | Adult male human whole-blood lymphocytes |
| **Metabolic Activation** | None |
| **Doses/Concentration** | 0.1, 0.5, 1, 5 & 10 mM |
| **Statistical Methods** | t-test |
| **Remarks for Test Conditions** | Vehicle was acetone |
| **Results** | No effects |
| **Cytotoxic concentration** | Approximately 5 mM |
| **Genotoxic Effects** | None |
| **Appropriate statistical evaluations?** | Yes |
| **Conclusion Remarks** | Phenethyl alcohol was unable to induce Sister-Chromatid Exchange in whole-blood lymphocyte cultures of a healthy male donor. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles. |
| **References** | Norppa H. and Vainio, H. (1983) Induction of sister-chromatid exchanges by styrene analogues in cultured human lymphocytes. Mutation Research, 116, 379-387. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | The test substance was phenylacetic acid, principal metabolite of phenethyl alcohol *in vivo*. |
| **Method/guideline** | Unscheduled DNA Synthesis Assay (UDS) |
| **Test Type** | Unscheduled DNA synthesis |
| **System of Testing** | Rat hepatocytes |
| **GLP** | Not given |
| **Year** | 1989 |
| **Species/Strain** | Rat/Fischer and Sprague-Dawley adult male |
| **Metabolic Activation** | No |
| **Doses/Concentration** | 1500 micrograms |
| **Statistical Methods** | Not given |

| | |
|---|---|
| **Remarks for Test Conditions** | Livers were perfused *in situ* with 0.5 mM EDTA in HEPES buffer (pH 7.2) for four minutes. Cultures of rat liver hepatocytes were incubated with the test material for 18-20 hours. UDS was measures by electronically counting nuclear grains and subtracting the average number of grains in 3 adjacent nuclear-sized cytoplasmic areas. 75-150 cells were analyzed for each dose level. The test was considered positive if an increase in net nuclear grain counts of at least six grains per nucleus above the solvent control and/or an increase in the percent of nuclei with at least 6 net grains to more than 10% above the negative control value. |
| **Results** | Negative at all dose levels |
| **Cytotoxic concentration** | Non-toxic at all dose levels |
| **Genotoxic Effects** | None |
| **Appropriate statistical evaluations?** | Not given |
| **Remarks for results** | The test article did not cause a significant increase in UDS as measured by the mean number of net nuclear grain counts by any dose level. The positive control, 7,12-dimethylbenz(a)-anthracene (DMBA), induced significant increases in the mean number of net nuclear grain counts compared to the solvent control. |
| **Conclusion Remarks** | There was no increase in unscheduled DNA synthesis. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles. |
| **References** | Heck J. D., Vollmuth, T. A., Cifone, M. A., Jagannath, D. R., Myhr B., and R.D. Curren (1989) An evaluation of food flavoring ingredients in a genetic toxicity screening battery. The Toxicologist, 9(1), 257. |

### 4.2.2 *In vivo* Genotoxicity

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Data for phenacetaldehyde, 2-methyl |
| **Method/guideline** | Sex linked recessive lethal mutation assay (Wuergler *et al*., 1977) |
| **Test Type** | Lethal mutation test |
| **GLP** | Ambiguous |
| **Year** | 1983 |

| | |
|---|---|
| **Species/Strain** | *Drosophila melanogaster* |
| **Sex** | Not reported |
| **Route of Administration** | Oral-Diet |
| **Doses/Concentration** | 10 mM |
| **Exposure Period** | Not reported |
| **Remarks for Test Conditions** | Flies were exposed to the test compound prepared in a 5% saccharose solution and 2% ethanol and 2% Tween 80 for compounds with poor water solubility. Further details of the methodology were not reported. |
| **Appropriate statistical evaluations?** | Yes. Statistical significance determined by methods of Kastenbaum and Bowman (1970). |
| **Effect on mitotic index or PCE/NCE ratio by dose level and sex** | Number of sex-linked lethal/chromosomes tested in Brood 1, 3/1187. Brood II, 2/650, and Brood III, 2/1180. |
| **Genotoxic effects** | None |
| **Remarks for Results** | Ten mM solutions of phenylacetaldehyde, 2-methyl did not increase the number of sex-linked recessive lethal mutations as compared to controls. |
| **Conclusion Remarks** | 10 mM solutions of phenylacetaldehyde, 2-methyl did not induce sex linked recessive lethals in *Drosophila melanogaster*. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restrictions. |
| **Remarks for Data Reliability** | Code 2. The data were acquired by standard methodology and published in a peer-reviewed journal but there was a limited description of the protocol and the results were tabulated. |
| **References** | Wild D., King, M.T., Gocke, E. and Eckhardt, K. (1983) Study of artificial flavouring substances for mutagenicity in the salmonella/microsome, basc and micronucleus tests. Fd Chem Toxicol., 21(6), 707-719. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Data for phenyacetic acid ester, isoeugenol phenylacetate |
| **Method/guideline** | Sex linked recessive lethal mutation assay (Wuergler *et al*., 1977) |
| **Test Type** | Lethal mutation test |
| **GLP** | Ambiguous |
| **Year** | 1983 |
| **Species/Strain** | *Drosophila melanogaster* |
| **Sex** | Not reported |

| | |
|---|---|
| **Route of Administration** | Oral-Diet |
| **Doses/Concentration** | 25 mM |
| **Exposure Period** | Not reported |
| **Remarks for Test Conditions** | Flies were exposed to the test compound prepared in a 5% saccharose solution and 2% ethanol and 2% Tween 80 for compounds with poor water solubility. Further details of the methodology were not reported. |
| **Appropriate statistical evaluations?** | Yes. Statistical significance determined by methods of Kastenbaum and Bowman (1970). |
| **Effect on mitotic index or PCE/NCE ratio by dose level and sex** | Number of sex-linked lethal/chromosomes tested in Brood 1, 6/1223. Brood II, 2/1097, and Brood III, 1/1200. |
| **Genotoxic effects** | None |
| **Remarks for Results** | Twenty-five mM solutions of phenylacetic acid, isoeugenol ester did not increase the number of sex-linked recessive lethal mutations as compared to controls. |
| **Conclusion Remarks** | Phenylacetic acid, isoeugenol ester did not induce sex linked recessive lethals in Drosophila melanogaster. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restrictions. |
| **Remarks for Data Reliability** | Code 2. The data were acquired by standard methodology and published in a peer-reviewed journal but there was a limited description of the protocol and the results were tabulated. |
| **References** | Wild D., King, M.T., Gocke, E. and Eckhardt, K. (1983) Study of artificial flavouring substances for mutagenicity in the salmonella/microsome, basc and micronucleus tests. Fd Chem Toxicol., 21(6), 707-719. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Data for phenacetaldehyde, 2-methyl |
| **Method/guideline** | Micronucleus test |
| **Test Type** | Clastogenic assay |
| **GLP** | Ambiguous |
| **Year** | 1983 |
| **Species/Strain** | Mouse/NMRI |
| **Sex** | Male and Female |
| **Route of Administration** | Intraperitoneal |
| **Doses/Concentration** | 134, 402, or 670 mg/kg bw in olive oil |

| | |
|---|---|
| **Exposure Period** | One dose at 0 hours |
| **Remarks for Test Conditions** | Groups of 10- to 14-week-old NMRI mice were intraperitoneally injected at 0 hours with 134, 402, or 670 mg/kg bw. At 30 hours, the mice were killed and bone marrow smears were prepared using the staining method of Schmid (1976). |
| **Appropriate statistical evaluations?** | Yes. Statistical significance determined by methods of Kastenbaum and Bowman (1970). |
| **Effect on mitotic index or PCE/NCE ratio by dose level and sex** | The mean number of micronucleated PE/1000 PE at 0, 134, 402, and 670 mg/kg bw was 1.5, 2.3, 1.3, and 2.5, respectively |
| **Genotoxic effects** | None |
| **Conclusion Remarks** | Phenylacetaldehyde, 2-methyl did not induce micronuclei in this assay. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. The data were acquired by standard methodology and published in a peer-reviewed journal but there was a limited description of the protocol and the results were tabulated. |
| **References** | Wild D., King, M.T., Gocke, E. and Eckhardt, K. (1983) Study of artificial flavouring substances for mutagenicity in the salmonella/microsome, basc and micronucleus tests. Fd Chem Toxicol., 21(6), 707-719. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Data for phenylacetic acid ester, isoeugenol phenylacetate |
| **Method/guideline** | Micronucleus test |
| **Test Type** | Clastogenic assay |
| **GLP** | Ambiguous |
| **Year** | 1983 |
| **Species/Strain** | Mouse/NMRI |
| **Sex** | Male and Female |
| **Route of Administration** | Intraperitoneal |
| **Doses/Concentration** | 564, 987, or 1,410 mg/kg bw in olive oil |
| **Exposure Period** | Two doses at 0 and 24 hours |
| **Remarks for Test Conditions** | Groups of 10- to 14-week-old NMRI mice were intraperitoneally injected at 0 and 24 hours with 564, 987, or 1,410 mg/kg bw. At 30 hours, the mice were killed and bone marrow smears were prepared using the staining method of Schmid (1976). |

| | |
|---|---|
| **Appropriate statistical evaluations?** | Yes. Statistical significance determined by methods of Kastenbaum and Bowman (1970). |
| **Effect on mitotic index or PCE/NCE ratio by dose level and sex** | The mean number of micronucleated PE/1000 PE at 0, 335, 670, and 1,005 mg/kg bw was 2.3, 1.3, 2.5, and 3.0, respectively. |
| **Genotoxic effects** | None |
| **Conclusion Remarks** | Phenylacetic acid, isoeugenol ester, did not induce micronuclei in this assay. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. The data were acquired by standard methodology and published in a peer-reviewed journal but there was a limited description of the protocol and the results were tabulated. |
| **References** | Wild D., King, M.T., Gocke, E. and Eckhardt, K. (1983) Study of artificial flavouring substances for mutagenicity in the salmonella/microsome, basc and micronucleus tests. Fd Chem Toxicol., 21(6), 707-719. |

## 4.3 Repeated Dose Toxicity

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Method/guideline** | Oral subchronic study |
| **GLP** | No |
| **Year** | 1981 |
| **Species/strain** | Rat |
| **Sex** | Male |
| **Route of Administration** | Oral-Gavage |
| **Doses/concentration Levels** | 51 mg/kg bw/day |
| **Exposure Period** | 4 months |
| **Frequency of Treatment** | Daily |
| **Remarks for test conditions** | Only liver function tests were conducted. |
| **Control Group** | Untreated |
| **Post Exposure** | None |
| **Toxic Response/effects by Dose Level** | Evidence of enzyme induction seen |
| **Data Qualities Reliabilities** | Reliability code 3. Not reliable. |

| | |
|---|---|
| **Remarks for Data Reliability** | Code 3. Does not meet important criteria of current standard methods. |
| **References** | Zaitsev A. N. and Rakhmanina N. L. (1974) Some data on the toxic properties of phenylethyl and cinnamyl alcohols. Voprosy pitaniia, 6, 48-53. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Data given for homologue phenethyl phenylacetate |
| **Method/guideline** | Oral subchronic study |
| **GLP** | No |
| **Year** | 1967 |
| **Species/strain** | Rat/Osborne Mendel |
| **Sex** | Male and Female |
| **Route of Administration** | Oral-Diet |
| **Doses/concentration Levels** | 0, 1,000, 2,500 or 10,000 ppm approximately an average daily intake of 0, 50, 125, or 500 mg/kg bw. |
| **Exposure Period** | 17 weeks |
| **Frequency of Treatment** | Daily |
| **Control Group** | Untreated diet |
| **Post Exposure** | None |
| **Remarks for Test Conditions** | Groups of ten male and ten female Osborne-Mendel rats were provided phenethyl phenylacetate in the diet at concentrations of 0, 1,000, 2,500 or 10,000 ppm which corresponds to an average daily intake of 0, 50, 125, or 500 mg/kg bw per day for 17 weeks. Measurements of body weight and food intake were recorded weekly. |
| **NOAEL (NOEL)** | 10,000 ppm or 500 mg/kg bw |
| **LOAEL (LOEL)** | None |
| **Actual dose received by dose level and sex** | Not reported |
| **Toxic Response/effects by Dose Level** | No effects at any dose |
| **Statistical Evaluation** | Not given |
| **Remarks for results** | Measurement of body weight and food intake recorded weekly showed no significant difference between test and control animals at any intake level. At termination, hematological examinations revealed no effects due to administration of the test substance. At necropsy, no differences were reported in |

| | |
|---|---|
| | major organ weights between test and control animals. Gross examination of tissue of all animals was unremarkable and histopathological examination of six-eight animals, equally represented by gender, for the high-dose group and the control group revealed no treatment-related lesions. |
| **Conclusion remarks** | The NOAEL was determined to be greater than 500 mg/kg bw/d. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Basic data given: comparable to guidelines/standards. |
| **References** | Hagan E. C., Hansen W. H., Fitzhugh O. G., Jenner P. M., Jones W. I., Taylor J. M., Long E. L., Nelson A. A. and Brouwer J. B. (1967) Food Flavourings and Compounds of related Structure. II. Subacute and Chronic Toxicity. Food and Cosmetic Toxicology, 5, 141-157. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Test substance was administered as a mixture and included 6,000 mg/kg bw ethyl alcohol (6%), 4 mg/kg bw ethyl acetate (0.004%), 120 mg/kg bw isoamyl alcohol (0.12%), 120 mg/kg bw phenethyl alcohol (0.12%), 200 mg/kg bw isobutyl alcohol (0.2%), and 200 mg/kg bw acetic acid (0.2%). |
| **Method/Guideline** | Oral subchronic study |
| **GLP** | No |
| **Year** | 1969 |
| **Species/strain** | Rats/Wistar |
| **Sex** | Male and Female |
| **Route of Administration** | Oral-drinking water |
| **Doses/concentration Levels** | 6,000 mg/kg bw ethyl alcohol (6%), 4 mg/kg bw ethyl acetate (0.004%), 120 mg/kg bw isoamyl alcohol (0.12%), 120 mg/kg bw phenethyl alcohol (0.12%), 200 mg/kg bw isobutyl alcohol (0.2%), and 200 mg/kg bw acetic acid (0.2%) |
| **Exposure Period** | 56 weeks |
| **Frequency of Treatment** | Daily |
| **Control Group** | Yes, tap water only |
| **Post Exposure** | None |
| **Remarks for Test Conditions** | Groups of male and female Wistar albino rats (20/sex/group) were given a mixture of compounds dissolved in tap water as their only drinking source for 56 weeks. This mixture included 6,000 mg/kg bw ethyl alcohol (6%), 4 mg/kg bw ethyl acetate (0.004%), 120 mg/kg bw isoamyl alcohol (0.12%), 120 mg/kg |

| | |
|---|---|
| | bw phenethyl alcohol (0.12%), 200 mg/kg bw isobutyl alcohol (0.2%), and 200 mg/kg bw acetic acid (0.2%). A control group of 20 rats/sex was maintained on tap water only. Body weights were recorded weekly. The activity of alcohol dehydrogenase (ADH), glutamic oxalacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), and the protein content were determined at two-four week intervals in the livers of rats. At study termination, liver, kidney, heart, spleen, and lung were examined histologically. |
| **Toxic Response/effects by Dose Level** | There was a slight non-statistically significant decrease in the mean body weight of the test groups at 28-29 weeks compared to 53-56 weeks. There was no difference in absolute or relative liver weight between the test and control groups. There was a slight increase in GOT activity between 28 and 56 weeks in the test and control groups. No significant abnormalities were observed in any of the organs examined. Six animals contracted pneumonia and were discarded. Pneumonia was common in the rats at termination, equally distributed in all groups. The authors concluded that the mixture of chemicals tested did not produce any effects in the parameters tested. |
| **Statistical Evaluation** | Yes, Kruskal-Wallis test |
| **Data Qualities Reliabilities** | Reliability code 3. Not reliable. |
| **Remarks for Data Reliability** | Code 3. Does not meet important criteria of current standard methods. |
| **References** | Johannsen E. and Purchase I.F.H. (1969) Kaffircorn malting and brewing studies. XXI: The effect of the fusel oils of Bantu beer on rat liver. S.A. Medical Journal (Supplement- S.A. Journal of Nutrition, 43(12), 326-328. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Purity 99.8% |
| **Method/Guideline** | Subchronic study |
| **GLP** | Ambiguous |
| **Year** | 1981 |
| **Species/strain** | Rat/Charles River CD |
| **Sex** | Male and Female |
| **Route of Administration** | Dermal |
| **Doses/concentration Levels** | 0.25, 0.5, 1.0 & 2.0 ml/kg bw/day |
| **Exposure Period** | 90 days |
| **Frequency of Treatment** | Daily |

| | |
|---|---|
| **Control Group** | Untreated |
| **Post Exposure** | None |
| **Remarks for Test Conditions** | Groups of Charles River CD albino rats were administered 0.25, 0.5, 1.0 and 2.0 ml/kg bw/d for 90 days. Material applied to the shaved dorsal. Animals were observed daily for appearance and behavior changes. Parameters evaluated weekly-included weight gain, food intake. Funduscopic and biomicroscopic examinations were performed on the eyes of all animals. Biochemical analyses were also performed. Necropsies were performed on all animals. |
| **NOAEL(NOEL)** | 0.5 ml/kg bw/day |
| **LOAEL (LOEL)** | 1.0 ml/kg bw/day |
| **Toxic Response/effects by Dose Level** | Significant decreases in body weight gain and body weights were reported for both sexes at the two highest dose levels. Decreased hemoglobin and white blood cell counts were reported for the high dose males only. No findings were reported upon histopathological examination. |
| **Statistical Evaluation** | Yes |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Basic data given: comparable to guidelines/standards. Published in a peer-reviewed journal. |
| **References** | Owston E., Lough R. and Opdyke D.L. (1981) A 90-day study of phenylethyl alcohol in the rat. Fd and Cosmet Toxicol, 19(6), 713-715. |

## 4.4 Reproductive Toxicity

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Data for principal animal metabolite, phenyl acetic acid |
| **Method/Guideline** | A 39-day reproduction/developmental-screening assay in SD rats. GLP Regs. FDA (1987) |
| **Test Type** | Reproductive/Developmental Toxicity Study |
| **GLP** | Yes |
| **Year** | 1990 |
| **Species/Strain** | Rat/Sprague-Dawley |
| **Sex** | Female/10/group |
| **Route of Administration** | Oral/gavage |

| | |
|---|---|
| **Duration of Test** | 39 days |
| **Doses/Concentration** | 250, 500 & 1000 mg/kg/day |
| **Premating Exposure period for males** | Not reported |
| **Premating Exposure period for females** | 7 days |
| **Control Group and Treatment** | Corn oil vehicle, 5 ml/kg/day |
| **Frequency of Treatment** | Daily |
| **Remarks for Test Conditions** | Virgin female Sprague-Dawley rats (10/group) were orally administered a vehicle or the test material at 3 dosages for one week prior to a 7-day cohabitation period through gestation, parturition and a 4-day postpartum period. Study duration was 39 days.<br><br>Maternal toxicity: Dams observed daily for clinical signs and were monitored for mortality, body weight, body weight gain, and food consumption. On day 25 of gestation dams were necropsied and examined for gross lesions. Reproductive performance was monitored in terms of mating index, fertility index, implantation sites per litter, duration of gestation, gestation index and litter size. |
| **NOAEL(NOEL)** | 250 mg/kg/d (maternal NOAEL) |
| **LOAEL(LOEL)** | 500 mg/kg/d (maternal LOAEL)) |
| **Appropriate statistical evaluations** | ANOVA followed by Dunnett's test |
| **Remarks for Results** | The decreased body weights and food consumption reported at 250 mg/kg bw/d during premating period were not considered adverse. Based on the significant decrease in (P less than 0.05) in pup weight at birth and pup viability in the high-dose group, the NOAEL for the F1 offspring was reported to be 500 mg/kg bw/day. |
| **Parental data and F1 as Appropriate** | Maternal changes at 250 mg/kg bw included a statistically significant decrease in body weight and body weight gain that was accompanied by a decrease in food consumption. At the 50 and 1000 mg/kg bw levels, a significant (P less than 0.05) increase in mortality, clinical symptoms of toxicity, and decreased body weight gain and food consumption were reported. At necropsy gross lesion of the liver and other organs was reported. Mating index was decreased in the 1000 mg/kg bw dose group only. In dams included decreased activity and excess salivation during the pre-gestation period and increased (P less than 0.01) salivation in the high dose group during gestation. Significant (P less than 0.05 to less than 0.01) decreases in body weight and absolute and relative food consumption were measured during the premating period. |
| **Offspring toxicity F1 and F2** | Significant (P less than 0.05) decrease in pup viability and body weight occurred in the high dose groups compared to controls. No gross lesions in pups were attributable to administration of |

| | |
|---|---|
| | the test material. |
| **Conclusion remarks** | The NOAEL for maternal toxicity was 250 mg/kg bw/day and the NOAEL for reproductive performance was 250 mg/kg bw/day. |
| **Remarks for Results** | |
| **Data Reliabilities Qualities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles. |
| **References** | Vollmuth T.A., Bennett, M.B., Hoberman, A.M. and Christian, M.S. (1995) An Evaluation of Food Flavoring Ingredients Using an In Vivo Reproductive and Developmental Toxicity Screening Test. Teratology, 41(5), 597. |

## 4.5 Developmental/Teratogenicity Toxicity

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Not characterized |
| **Test Type** | Fetal developmental study |
| **GLP** | No |
| **Year** | 1983 |
| **Species/strain** | Rat/Long-Evans |
| **Sex** | Female |
| **Route of Administration** | Oral-Gavage |
| **Duration of Test** | 20 days |
| **Doses/concentration Levels** | 0, 4.3, 43 & 430 mg/kg bw/d |
| **Exposure Period** | Days 6 - 15 of gestation |
| **Frequency of Treatment** | Daily |
| **Control Group and Treatment** | Vehicle (water) only |
| **Remarks for Test Conditions** | The test material was dosed as an aqueous suspension. 19 rats in control group, 7 in low and mid-dose groups and 5 in high dose. |
| **NOAEL(NOEL) maternal toxicity** | 43 mg/kg |
| **LOAEL(LOEL) maternal toxicity** | 430 mg/kg |

| | |
|---|---|
| **toxicity** | |
| **LOAEL (LOEL) developmental toxicity** | 4300 mg/kg |
| **Actual dose received by dose level and sex** | Not given |
| **Maternal data with dose level** | "Severe intoxication" at high dose and asymtomatic at 2 lower doses. |
| **Fetal Data with Dose Level** | The average birth weight and pup size of all treated groups were significantly lower than those of the control group, but the change was not dose-related. In fact, birth weights were greater in the mid-dose group than in controls. Mean litter size was greater in the high dose group (13) than in either the two lower doses (9) or controls (12). Also, embryolethality did not occur in the high dose group but was 18% at 43 mg/kg and 10% at 4.3 mg/kg. The authors reported a clear dose related increase in the percentage of malformations in live offspring (100% at the 432 mg/kg level, 93% at 43 mg/kg and 50% at 4.3 mg/kg). Malformations were mainly in ocular malformation, neural tube defects, hydronephrosis and limb defects. |
| **Appropriate statistical evaluations** | Yes |
| **Remarks for Results** | Dose response evident only on grouping of certain malformations. Often no dose response on individual effects or by grouping related effects. |
| **Data Qualities Reliabilities** | Reliability code 3. Not reliable. |
| **Remarks for Data Reliability** | Code 3. Documentation insufficient for assessment. |
| **References** | Mankes R. F., LeFevre R., Bates H. and Abraham R. (1983) Effects of Various Exposure Levels of 2-Phenylethanol on Fetal Development and Survival in Long-Evans Rats. Journal of Toxicology and Environmental Health, 12, 235-244. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Purity 98.5% |
| **Method/Guideline** | Modified OECD 414 |
| **Test Type** | Prenatal developmental |
| **GLP** | Yes |
| **Year** | 1986 |
| **Species/strain** | CrL:COBS CD (SD) BR |
| **Sex** | Female |
| **Route of Administration** | Dermal |

| | |
|---|---|
| **Duration of Test** | 21 days |
| **Doses/concentration Levels** | 140, 430 & 1400 mg/kg |
| **Exposure Period** | Days 6-15 of pregnancy |
| **Frequency of Treatment** | Daily |
| **Control Group and Treatment** | Water |
| **Remarks for Test Conditions** | Test was conducted according to OECD 414 except dosing was only during the period of organogenesis. The effect of phenethyl alcohol on pregnancy of rats was studied (Palmer *et al*., 1986). Phenethyl alcohol was applied topically at the dose of 0, 0.14, 0.43 or 1.40 ml/kg (approximately 143, 438, or 1430 mg/kg bw) during day 6 to 15 of pregnancy. The doses are approximately equal to 0, 140, 430, and 1400 mg/kg bw, respectively, and were chosen so that the intermediate dose was roughly equivalent to the highest dosage used in a previous oral study (Mankes *et al*., 1983). The highest dose was designed to extend the range in case of differential absorption by the dermal route. The animals were killed on day 20 of pregnancy and in utero development assessed by determination of litter values and examination of the fetuses for soft tissue and skeletal changes. |
| **NOAEL(NOEL) maternal toxicity** | 430 mg/kg |
| **LOAEL(LOEL) maternal toxicity** | 1400 mg/kg |
| **NOAEL (NOEL) developmental toxicity** | 140 mg/kg |
| **Actual dose received by dose level and sex** | 430 mg/kg |
| **Maternal data with dose level** | 1400 mg/kg death of 3/35 and suppression of food intake and growth rate with clinical signs of toxicity.<br>No significant effects at lower doses |
| **Fetal Data with Dose Level** | 1400 mg/kg resorption of 5/23 litters, reductions in litter size and weight. Morphological change in 160/161 foetuses.<br>430 mg/kg increased incidence of foetuses with cervical rib bud and defects of thoracic vertebrae<br>140 mg/kg, no significant effects. |
| **Appropriate statistical evaluations** | Yes |
| **Remarks for Results** | Although fetal effects at 430 mg/kg were not considered serious according to the authors, this dose cannot be called a NOAEL. |
| **Data Qualities Reliabilities** | Reliability code 1. Reliable without restriction. |
| **Remarks for Data Reliability** | Code 1. Comparable to guideline study. |
| **References** | Palmer A.K., Bottomley, A. M., Ratcliffe, H.E. Clark, R., and John, D. M. (1986) Effect of Phenylethyl Alcohol (PEA) on |

Pregnancy of the Rat. Huntingdon Research Center. Unpublished report to RIFM.

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Purity 99.6% |
| **Test Type** | Prenatal developmental dosage-range toxicity study |
| **GLP** | Yes |
| **Year** | 1986 |
| **Species/strain** | CrL:COBS CD (SD) BR |
| **Sex** | Female |
| **Route of Administration** | Dermal |
| **Duration of Test** | 21 days |
| **Doses/concentration Levels** | 70, 140, 280, 430 & 700 mg/kg |
| **Exposure Period** | Days 6-15 of pregnancy |
| **Frequency of Treatment** | Daily |
| **Control Group and Treatment** | Water |
| **Remarks for Test Conditions** | The test was conducted as a follow-up to Palmer, *et al.*, 1986 to better define the fetal and maternal NOAELs. |
| **NOAEL(NOEL) maternal toxicity** | Less than 70 mg/kg |
| **LOAEL(LOEL) maternal toxicity** | 70 mg/kg |
| **NOAEL (NOEL) developmental toxicity** | 140 mg/kg |
| **Actual dose received by dose level and sex** | 280 mg/kg |
| **Maternal data with dose level** | Signs of dermal irritation were seen in all dosed groups. |
| **Fetal Data with Dose Level** | The NOEL for the cervical rib formation seen in Palmer *et al.* 1986 was 430 mg/kg. Other effects including incomplete ossification and decreased fetal body weight possibly as an indirect result of the maternal irritation were seen in all dose groups but were considered reversible effects. The only statistically significant difference from controls in the two lower dose groups was incomplete ossification of the pelvis but with no dose correlation. |
| **Appropriate statistical evaluations** | Yes |

| | |
|---|---|
| **Conclusion Remarks** | The study was compromised due to the dermal irritation seen at all dose levels. |
| **Data Qualities Reliabilities** | Reliability code 2. Reliable with restriction. |
| **Remarks for Data Reliability** | Code 2. Comparable to guideline study with acceptable restrictions. |
| **References** | Christian M.S. and Hoberman A.M. (1988) Dosage-range developmental toxicity (embryo/fetal toxicity and teratogenicity) study of 2-phenylethylalcohol (PEA) administered dermally to presumed pregnant mice. Unpublished report to RIFM |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Data for principal animal metabolite, phenylacetic acid |
| **Method/Guideline** | A 39 day reproduction/developmental screening assay in SD rats. GLP Regs. FDA (1987) |
| **Test Type** | Virgin female Sprague-Dawley rats (10/group) were orally administered a vehicle or the test material at 3 dosages for one week prior to a 7-day cohabitation period through gestation, parturition and a 4-day postpartum period. Study duration was 39 days. |
| **GLP** | Yes |
| **Year** | 1990 |
| **Species/strain** | Rat/Sprague-Dawley |
| **Sex** | Female/10/group |
| **Route of Administration** | Oral-Gavage |
| **Duration of Test** | 39 days |
| **Doses/concentration Levels** | 250, 500 & 1000 mg/kg/day |
| **Exposure Period** | 7 days premating, through gestation and 4 days postpartum (39 days) |
| **Frequency of Treatment** | Daily |
| **Control Group and Treatment** | Corn oil vehicle, 5 ml/kg/day |
| **Remarks for Test Conditions** | Virgin female Sprague-Dawley rats (10/group) were orally administered a vehicle or the test material at 3 dosages for one week prior to a 7-day cohabitation period through gestation, parturition and a 4-day postpartum period. Study duration was 39 days. Developmental toxicity was monitored in terms of mortality, viability (pups dying on days 1-4), pup body weight and pup body weight gain. |
| **NOAEL(NOEL) maternal toxicity** | 250 mg/kg bw |

| | |
|---|---|
| **LOAEL(LOEL) maternal toxicity** | 500 mg/kg bw |
| **NOAEL (NOEL) developmental toxicity** | 500 mg/kg bw |
| **LOAEL(LOEL) developmental toxicity** | 1000 mg/kg bw |
| **Maternal data with dose level** | Maternal changes at 250 mg/kg bw included a statistically significant decrease in body weight and body weight gain that was accompanied by a decrease in food consumption. At the 500 and 1000 mg/kg bw levels, a significant (P less than 0.05) increase in mortality, clinical symptoms of toxicity, and decreased body weight gain and food consumption (P less than 0.05) were reported. At necropsy gross lesions of the liver and other organs were reported. Mating index was decreased in the 1000 mg/kg bw dose group only. Effects in dams included decreased activity and excess salivation during the pre-gestation period and increased (P less than 0.01) salivation in the high dose group during gestation. Significant (P less than 0.05 to less than 0.01) decreases in body weight and absolute and relative food consumption were measured during the premating period. |
| **Fetal Data with Dose Level** | No effects on development were observed at 250 or 500 mg/kg bw. Offspring effects observed only at the highest dose included a statistically significant (P less than 0.05) decrease in viability and a non-significant decrease in body weight gain. |
| **Appropriate statistical evaluations** | ANOVA followed by Dunnett's test |
| **Remarks for Results** | The decreased body weights and food consumption reported at 250 mg/kg bw/d during premating period were not considered adverse. Based on the significant decrease in (P less than 0.05) in pup viability in the high-dose group, the NOAEL for the F1 offspring was reported to be 500 mg/kg bw/day. |
| **Conclusion Remarks** | The NOAEL for development of offspring is 500 mg/kg bw/day. |
| **Data Qualities Reliabilities** | Reliability code 1. Reliable without restriction. |
| **Remarks for Data Reliability** | Code 1. Comparable to guideline study. |
| **References** | Vollmuth T.A., Bennett, M.B., Hoberman, A.M. and Christian, M.S. (1995) An Evaluation of Food Flavoring Ingredients Using an In Vivo Reproductive and Developmental Toxicity Screening Test. Teratology 41(5), 597. |

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Remarks for Substance** | Blended commercial sample, purity 98.5%, from 4 manufacturers spray dried with gum Arabic at a concentration of 17.6%. |
| **Method/Guideline** | Essentially the same as OECD 414 except dosing was on days 6 – 16 of pregnancy. |

| | |
|---|---|
| | 6 – 16 of pregnancy. |
| **Test Type** | Prenatal Developmental Toxicity Study |
| **GLP** | Yes |
| **Year** | 1987 |
| **Species/strain** | CrL: COBS CD(SD)BR rats |
| **Sex** | Female |
| **Route of Administration** | Oral-Diet |
| **Duration of Test** | 20 days |
| **Doses/concentration Levels** | 0, 1000, 3000 & 5000 ppm resulting in intakes of about 83, 266 & 799 mg/kg/day. |
| **Exposure Period** | Days 6-15 of pregnancy |
| **Frequency of Treatment** | Daily |
| **Control Group and Treatment** | Gum Arabic |
| **Remarks for Test Conditions** | Microencapsulation in Gum Arabic was used to prevent decreased food intake due to inappetence. Bioavailability was demonstrated in separate study (Hawkins *et al*., 1990). |
| **NOAEL(NOEL) maternal toxicity** | 5000 ppm |
| **LOAEL(LOEL) maternal toxicity** | None |
| **NOAEL (NOEL) developmental toxicity** | 5000 ppm |
| **LOAEL(LOEL) developmental toxicity** | None |
| **Actual dose received by dose level and sex** | Mean daily intakes during days of dosing were 83.1, 265.9 & 799.1 mg/kg. |
| **Maternal data with dose level** | No effects at any dose. |
| **Fetal Data with Dose Level** | No effects at any dose. |
| **Appropriate statistical evaluations** | Yes |
| **Remarks for Results** | The study was conducted to determine the effect of route of dosing on developmental toxicity. |
| **Conclusion Remarks** | There was no evidence of maternal or fetal toxicity at any dose level after dietary administration. |
| **Data Qualities Reliabilities** | Reliability code 1. Reliable without restriction. |
| **Remarks for Data Reliability** | Code 1. Comparable to guideline study. |
| **References** | Bottomley A. M., Ratcliffe H. E., John D. M., Anderson A., Dawe I. S. (1987) Effect of Dietary Administration of Micro- |

Encapsulated Phenylethyl Alcohol on Pregnancy of the Rat (Embryotoxicity Study). Unpublished Report to RIFM.

| | |
|---|---|
| **Substance Name** | Phenethyl alcohol |
| **CAS No.** | 60-12-8 |
| **Test Type** | Embryotoxicity |
| **GLP** | No |
| **Year** | 1973 |
| **Species/strain** | Rats/Mongrel white |
| **Sex** | Female |
| **Route of Administration** | Oral-Gavage |
| **Duration of Test** | 20 days |
| **Doses/concentration Levels** | 508 mg/kg |
| **Exposure Period** | Once on 4th day of pregnancy or once during 10-12th day. |
| **Frequency of Treatment** | Once |
| **Control Group and Treatment** | Solvent only |
| **Remarks for Test Conditions** | Administered in sunflower oil. |
| **Actual Dose Received by Dose Level and Sex** | 508 mg/kg |
| **Maternal data with Dose Level** | No maternal data reported |
| **Fetal Data with Dose Level** | Single dose level of 508 mg/kg caused no effects when administered at the 4th day of pregnancy but caused slight retardation of ossification when administered during the 10-12th day. |
| **Appropriate Statistical Evaluations** | Not reported |
| **Remarks for Results** | While study is poorly reported, results are consistent with other studies. |
| **Data Qualities Reliabilities** | Reliability code 3. Not reliable. |
| **Remarks for Data Reliability** | Code 3. Method not validated. |
| **References** | Maganova N.B. and Zaitsev A.N. (1973) Study of the Embryotoxic Action of Some Synthetic Food Flavourings. Vopr Pitan, 32(4), 50-54. |